# MULTICENTER, OPEN-LABEL, RANDOMIZED NON-INFERIORITY STUDY COMPARING 8-WEEK VS 12-WEEK SOFOSBUVIR/RAVIDASVIR TREATMENT FOR NON-CIRRHOTIC CHRONIC HEPATITIS C PATIENTS (EASE TRIAL)


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## 1 | BACKGROUND AND AIMS

Hepatitis C virus (HCV) remains a significant global health challenge, exacerbated by high treatment costs associated with direct-acting antivirals (DAAs). There is a pressing need for more affordable and efficient treatment options. **This study compared the effectiveness of an 8-week versus a 12-week regimen of sofosbuvir/ravidasvir in non-cirrhotic patients with chronic HCV infection.**

## 2 | METHOD

- A **randomized, open-label, non-inferiority** clinical trial was conducted in 26 sites involving public hospitals and primary care centers in Malaysia. Non-cirrhotic adults with chronic HCV of all genotypes were **randomly assigned (1:1)** to receive either 8 or 12 weeks of sofosbuvir/ravidasvir using a **permuted block randomization**.
- **Primary Endpoint :** Sustained virologic response 12 weeks post-treatment (SVR12).
- **Secondary Endpoints :**
- (1) Factors associated with SVR12 achievement across demographic and clinical subgroups and
- (2) incidence of treatment-emergent adverse events (TEAEs).
- Data imputation was not performed, as the proportion of missing or unavailable SVR12 values was within the pre-specified acceptable threshold of 10%. Non-inferiority was established with a 5% margin, and analysis was conducted using the intention-to-treat population.
- The study protocol was approved by Malaysia Medical Research and Ethics Committee (MREC) (NMRR-20-328-52925) and was registered with ClinicalTrials.gov (NCT04885855).

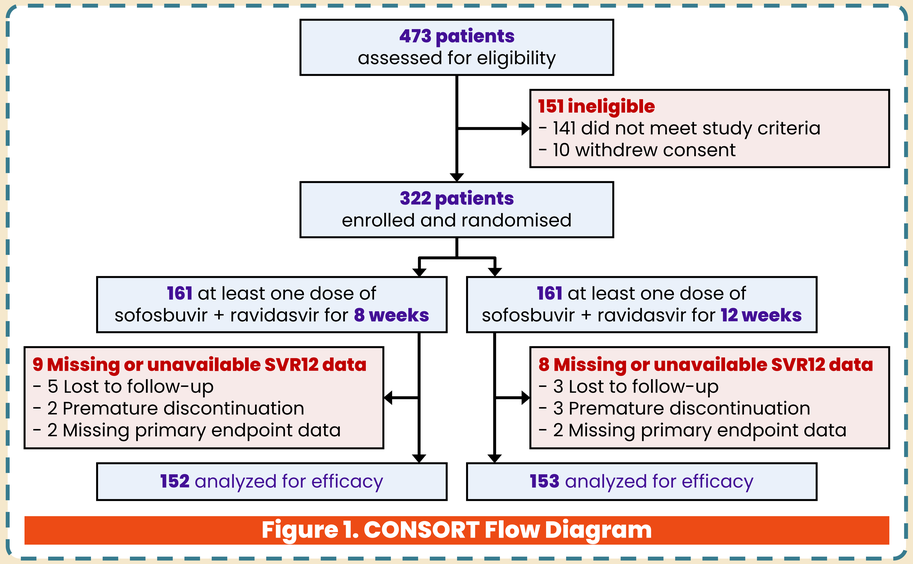


Figure 1. CONSORT Flow Diagram

## 3 | RESULTS

- A total of 322 participants were randomized to either the 8-week (n=161) or 12-week (n=161) regimen. The majority of participants were aged 40–49 years (42.2% vs. 41.0%) had at least secondary education (77.0% vs 79.5%) and had body mass index of <30 kg/m2 (91.3% vs 91.3%).
- **Primary Endpoint:** The 8-week regimen achieved an SVR12 rate of 93.42% (142/152), while the 12-week regimen had an SVR12 rate of 93.46% (143/153), **demonstrating non-inferiority (difference: -0.04%; 90% CI: -4.94%, 4.85%; p-value = 0.047)**.
- **Secondary Endpoint:**
- (1) There is no factors associated with the SVR12 achievement.
- (2) Adverse events were similar between both treatment groups, with hypertension (6.2% vs. 5.6%), headache (2.5% in both groups), and arthralgia (0.6% vs. 3.1%) being the most common.

**Table 1. Clinical characteristics between 8-week and 12-week groups**

| Variables | 8-week group (N = 161) n(%) | 12-week group (N = 161) n(%) | Total (N = 322) n(%) |
|---|---|---|---|
| **HCV RNA (IU/mL)** | | | |
| < 800,000 | 55 (34.16) | 62 (38.51) | 117 (36.34) |
| ≥ 800,000 | 106 (65.84) | 99 (61.49) | 205 (63.66) |
| **Genotype** | | | |
| Genotype 1 | 54 (33.96) | 47 (29.38) | 101 (31.66) |
| Genotype 3 | 94 (59.12) | 99 (61.88) | 193 (60.50) |
| Other | 10 (6.29) | 10 (6.25) | 20 (6.27) |
| **HIV status** | | | |
| HIV Positive | 9 (5.59) | 12 (7.45) | 21 (6.52) |
| HIV Negative | 152 (94.41) | 149 (92.55) | 301 (93.48) |
| **HIV-1 RNA viral load (copies/mL)** | | | |
| < 20 | 8 (4.97) | 10 (6.21) | 18 (5.59) |
| ≥ 20 | 1 (0.62) | 2 (1.24) | 3 (0.93) |
| **CD4/CD8 count (cells/mm³)** | | | |
| < 400 | 4 (2.48) | 4 (2.48) | 8 (2.48) |
| ≥ 400 | 5 (3.11) | 8 (4.97) | 13 (4.04) |
| **Adherence** | | | |
| < 90% (SOF/RDV) | 2 (1.24) | 5 (3.11) | 7 (2.17) |
| ≥ 90% (SOF/RDV) | 158 (98.14) | 156 (96.89) | 314 (97.52) |

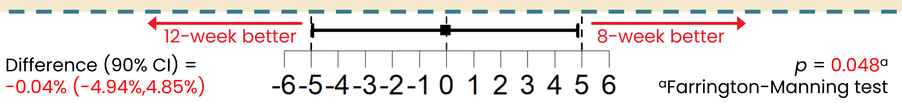


Figure 2. SVR12 rate between 8-week and 12-week groups (ITT Population)

**Table 2. Factors associated with SVR12 achievement (Multiple Logistic Regression)**

| Variables | Adj. OR(95% CI) | p-value[a] |
|---|---|---|
| **Group** | | |
| 8-week group vs 12-week group (ref.) | 1.05(0.39,2.83) | 0.919 |
| **HCV-RNA Result at Baseline** | | |
| < 800,000 vs ≥ 800,000 (ref.) | 1.11(0.38,3.24) | 0.849 |
| **HIV Status** | | |
| Positive vs Negative (ref.) | 2.67(0.25,28.39) | 0.416 |
| **HCV Genotype** | | |
| Genotype 1 vs Others (ref.) | 4.48(0.75,26.61) | 0.099 |
| Genotype 3 vs Others (ref.) | 5.04(0.96,26.61) | 0.057 |
| **Injection Drug Use** | | |
| Yes vs No (ref.) | 1.31(0.30,5.68) | 0.715 |
| **Diabetes** | | |
| Yes vs No (ref.) | 0.45(0.07,3.06) | 0.414 |
| **Hypertension** | | |
| No vs Yes (ref.) | 1.53(0.43,5.48) | 0.511 |

Note: [a]Multiple Logistic Regression using the Enter method, adjusted by Age ($p$ = 0.585), Sex ($p$ = 0.821), Ethnicity ($p$ = 0.996), Employed ($p$ = 0.493), Unemployed ($p$ = 0.101), Primary Education ($p$ = 0.866), Secondary Education ($p$ = 0.793), Body Mass Index ($p$ = 0.079), Adherence Rate ($p$ = 0.084), APRI Score ($p$ = 0.711), Tattooing ($p$ = 0.840), Body Piercing ($p$ = 0.795), Prisoner ($p$ = 0.539); ref. = Reference category; Adj. OR (95% CI) = Adjusted Odds Ratio (95% Confidence Interval).

## 4 | CONCLUSION

The 8-week sofosbuvir/ravidasvir treatment regimen demonstrated non-inferior efficacy compared to the 12-week regimen, indicating that it could be a shorter, more cost-effective option for treating non-cirrhotic individuals with chronic HCV infection potentially for challenging populations, such as PWID/ incarcerated inmates.

## 5 | ACKNOWLEDGEMENT


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## 6 | REFERENCES


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